

***THIS OPINION WAS NOT WRITTEN FOR PUBLICATION***

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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***Ex parte*** ERHARD KOPETZKI and  
GUNTHER SCHUMACHER

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Appeal No. 1995-1162  
Application 07/725,943<sup>1</sup>

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ON BRIEF

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Before DOWNEY, WILLIAM F. SMITH and ELLIS, ***Administrative Patent Judges***.

ELLIS, ***Administrative Patent Judge***.

***DECISION ON APPEAL***

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 12, 15, 18, 19 and 21 through 35, all the claims remaining in the application.

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<sup>1</sup>Application for patent filed June 27, 1991. According to the appellants, this application is a continuation of Application 07/215,724, filed July 6, 1988, now abandoned.

Claims 1, 21, and 35 are illustrative of the subject matter on appeal; they read as follows:

1. In a process for the expression of a protein in a transformed ***Escherichia coli*** host cell containing DNA sequence encoding said protein and controlled by an inducible promoter, said process comprising limiting induction of said promoter to less than 10% of the maximum induction of said promoter and being effective to reduce the rate of transcription of said DNA encoding said protein and thereby to reduce the rate of synthesis of said protein to thus produce a greater amount of soluble and/or active protein than in the absence of said limited induction of said promoter.

21. The process according to claim 1 wherein the maximum induction of said promoter is determined by comparison with a standard system of said transformed host cell, wherein said standard system consists of the expression of beta-galactosidase in said host cell under the control of the same promoter as a foreign gene and with an inducer concentration of 0.1 to 1 mmol/l IPTG.

35. Process of claim 21, wherein said promoter has a catabolite activator protein site and said promoter has reduced affinity for said catabolite activator protein.

The references relied upon by the examiner are:

Dennis N. Luck et al. (Luck), "Synthesis of Bovine Prolactin in ***Escherichia coli***," ***Biochem. J.***, Vol. 5, no. 1, pp. 21-28 (November 1, 1986).

Miroslawa M. Bagdasarian et al. (Bagdasarian), "Activity of the Hybrid ***trp-lac(tac)*** Promoter of ***Escherichia coli*** in ***Pseudomonas putida***. Construction of Broad-Host-Range, Controlled-Expression Vectors," ***Gene***, Vol. 26, pp. 273-282 (1983).

Ernst-Ludwig Winnacker (Winnacker), "Expression Vectors in Prokaryotes," In: ***From Genes to Clones: Introduction to Gene Tech.***, Publishers: VCH (1987), 239-317.

The claims stand rejected as follows:

I. Claims 1 through 12, 15, 18, 19 and 21 through 35 stand rejected under 35 U.S.C. § 112, first paragraph as being enabled “only for claims limited to the expression of alpha-glucosidase in *E. coli* utilizing a *lac* inducible promoter and a *lacI<sup>r</sup>* gene.”

Answer, p. 3.

II. Claim 35 stands rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable one skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter of the invention.

III. Claims 1 through 12, 15, 18, 19 and 21 through 35 stand rejected under 35 U.S.C. § 103 as being unpatentable over Luck or Bagdasarian in view of Winnacker.

We **reverse**.

### **§ 112 First and Second Paragraph Issues**

In the case before us, the examiner first contends that “[t]he specification does not contemplate nor accommodate any and all proteins expressed by a transformed *E. coli*.”

Answer, p. 4. The examiner then proceeds to make a series of statements about inducible promoters and protein expression, folding and size. Presumably, these statements form

the basis of the examiner's conclusion that the "specification does not provide one of ordinary skill in the art with the guidance to practice applicants' invention without undue experimentation." *Id.*, sentence bridging pp. 4-5.

In addition, the examiner argues that claim 35 fails to satisfy the requirements of both the first and second paragraphs of 35 U.S.C. § 112. According to the examiner, the "Appellants do not provide any guidance as to the meaning of the phrase or what promoters and proteins are encompassed by the terms." Answer, p. 5.

In response, the appellants argue that inducible promoters were well known in the art at the time the application was filed, and they provide five references to support their position. Brief, pp. 10-11; Exhibits A through F. With respect to claim 35, the appellants contend that they explain "the limitation of promoter induction to the recited degree via altered affinity for an activator protein," in detail on p. 6 of their brief. Brief, p. 13.

We acknowledge that in unpredictable art areas, our appellate reviewing court has "refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim." *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996). The court explained that enablement is lacking in those cases, "because the undescribed embodiments cannot be made, based on the disclosure

in the specification without undue experimentation.” *Id.* The court has further explained that the

factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd. Pat. App. & Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims [*In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)].

On this record, we find the examiner’s initial rejection of all the claims under § 112, first paragraph, to be tantamount to an assertion that one skilled in the art can not make and use the claimed invention throughout its scope without undue experimentation. The mere citing of a series of facts, without relating them to the criteria for determining undue experimentation set forth in *In re Wands*, is not sufficient to establish a *prima facie* case of nonenablement.

Moreover, nowhere in her two paragraph “Response to Arguments” [Answer, pp. 7-8], does the examiner acknowledge (i) the appellants’ arguments as to what was known in the art with respect to inducible promoter systems, and (ii) the references relied upon to support those arguments. Thus, we find that the examiner has erred in failing to indicate whether she entered and considered any of the references accompanying the brief<sup>2</sup> and, if

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<sup>2</sup> We note that two of the references; i.e., Exhibits E and F, are in German. The appellants have failed to provide, and the examiner has not requested, certified

they were entered and considered, what her substantive response is.

As to claim 35, we note that it is dependent upon claim 21, which in turn is dependent upon claim 1. See p. 2, above. Thus, claims 1 and 21 manifestly encompass embodiments which possess the limitations set forth in claim 35. Accordingly, it logically follows that if claim 35 fails to satisfy the requirements of the first and second paragraphs of §112, claims 1 and 21 also fail to satisfy these requirements. Since the examiner has erred in failing to include all the relevant claims in the rejection, we are constrained to reverse. Moreover, we point out that here, too, the examiner has erred in not responding to the appellants' arguments with respect to claim 35. Brief, p. 13.

Since neither rejection is based upon the correct legal standards and the examiner has not acknowledged and responded to the appellants' arguments, we reverse.

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translations thereof.

### **Obviousness**

The examiner has premised her conclusion of obviousness on the teachings of Luck, Bagdasarian and Winnacker. The examiner argues that:

the references cited clearly teach that regulation of protein expression by an inducible promoter is an old process. To the extent that specific limitations are not taught, these limitations would have been obvious to one skilled in the art at the time of applicants' invention [Answer, p. 7].

It is well established that the examiner has the initial burden under § 103 to establish a **prima facie** case of obviousness. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); *In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984). To that end, the examiner must show that some objective teaching or suggestion in the applied prior art, or knowledge generally available in the art would have led one of ordinary skill in the art to lead combine the references to arrive at the claimed invention. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996). Here, we do not find that the examiner has even begun to provide reasons, based on the applied prior art or otherwise, as to why it would have been obvious to one of ordinary skill in the art to limit the induction of the inducible promoter in the manner required by the claims in order to produce greater amounts of soluble protein in a transformed *E. coli* host cell. As developed in the appellants' brief, the references do not even allude to the solubility of the protein expression products described therein. We remind the examiner that a conclusion of

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obviousness cannot be based on generalities. *In re Warner*, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), **cert. denied**, 389 U.S. 1057 (1968); *In re Freed*, 425 F.2d 785, 788, 165 USPQ 570, 571 (CCPA 1970). Accordingly, absent a fact-based explanation from the examiner as to why the applied prior would have rendered the claimed subject matter obvious to one of ordinary skill in the art, we must reverse the rejection.

The decision of the examiner is reversed.

**REVERSED**

MARY F. DOWNEY	)	
Administrative Patent Judge	)	
	)	
	)	
WILLIAM F. SMITH	)	BOARD OF PATENT
Administrative Patent Judge	)	APPEALS AND
	)	INTERFERENCES
	)	
JOAN ELLIS	)	
Administrative Patent Judge	)	

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